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Medical Journal, 1970). The immunosuppressive effects of corticosteroids are well known and these steroids are used extensively for this purpose in tissue transplantation. It is likely that androsterone may enhance the immune response because of its anabolic effects. Thus, the high 17-OHcs : A ratio seen in patients with a poor prognosis may lead to a reduced immune response against the tumour.

It must be emphasized that although the above mechanisms are discussed separately two or more of these may be operating in unison to enhance the effect of steroid abnormalities. A careful investigation of these mechanisms in the prognosis of cancer would be a rewarding study.

A convincing method of proving that the steroid abnormalities in lung cancer are of aetiological significance would be to study the effects of correction of these abnormalities on the prognosis of these patients. Since the abnormalities in steroid excretion centre around a deficiency of androsterone these could be corrected by the administration of this steroid or a suitable precursor. Testosterone would not be a suitable steroid because the A : E ratio is not altered by its administration (Johnsen, 1968). Dehydroepiandrosterone also would not be a suitable precursor because this steroid is converted mainly to aetiocholanolone and thus would increase the abnormality found in lung cancer (Kirschner and Lipsett, 1964). It may therefore be necessary to administer androsterone or some other 5-alpha-androstane compound. Since the correction of the deficiency of androsterone could be carried out in conjunction with the existing methods of therapy it should be entirely feasible to conduct such a clinical trial.

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PREDICTION OF 1-YEAR SURVIVAL AFTER RESECTION OF LUNG TUMOURS FROM THE PREOPERATIVE STEROID EXCRETION PATTERN

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SUMMARY

A prospective study of 50 patients with lung cancer who were treated by surgical resection of their tumour has shown that most of those who died within 1 year after resection had abnormalities in preoperative steroid excretion whereas most of those who are alive had normal steroid excretion. Of the 21 patients who died within 1 year, 5 died in hospital, mainly as a result of surgical complications, and were found to have an abnormally low androsterone to aetiocholanolone ratio and a high total 17-oxosteroid excretion. Those who were discharged alive and well from hospital but who died within 1 year as a result of metastasis to other organs had a low androsterone level in relation to aetiocholanolone and to total 17-hydroxycorticosteroids. Thus, it has been possible to identify by their preoperative steroid excretion 12 out of 14 patients who died within 1 year although they had had a successful resection.

ALTHOUGH radical surgery offers the best chance of survival for patients with lung cancer compared with other methods of treatment, nearly half of the surgically treated patients die within 1 year. Therefore a method of prediction of the prognosis might be useful for the management of these patients. If the technique of prediction has a biochemical basis it might provide clues to the pathogenesis of this disease and might even lead to a therapeutic application. Such a chemical method of predicting prognosis has already been shown to be effective for patients with inoperable lung cancer (Rao and Hewit, 1970). The present report deals with the prognosis of patients whose lung tumours have been resected by a lobectomy or pneumonectomy.

PATIENTS AND METHODS

Fifty male patients, aged 36–68 years (mean 55·7 years), who had undergone a resection of their lung tumour were followed up for a period of at least 1 year from the date of surgery; 27 had had a pneumonectomy and 23 a lobectomy. Two early morning specimens of urine had been collected for steroid assay about 3 days before surgery. Details of patients and laboratory methods have been described elsewhere (Rao, 1970).

RESULTS

Twenty-one patients died within 1 year after resection and, of these, 5 died in hospital mainly as a result of surgical complications such as haemoptysis, peripheral shock, or pulmonary embolism (group 1). Of the remaining 16 patients, 2 died of heart failure and kidney failure 4 and 7 months respectively after surgery and had no obvious evidence of metastases. The remaining 14 patients left hospital after surgery in a reasonable condition but died within 1 year mainly as a result of metastasis to the other lung or to other organs (group 2). Twenty-nine of the patients were alive and most of these were well 1 year after resection (group 3). Steroid excretion before resection was compared in the three groups and showed some striking differences (*Table I*). Among the patients who died within 1 year, those who died in hospital showed some differences in steroid excretion compared with those who left hospital alive and well; the former patients had a lower androsterone (A) to aetiocholanolone (E) ratio than the mean for group 2, and they also had higher 17-oxosteroid (KS) and 17-hydroxycorticosteroid (17-OHcs) excretion levels compared with those in groups 2 and 3. Patients in group 2 had significantly lower excretion of A and E compared with that in group 3. In group 2, 12 out of 14 patients had a 17-OHcs : A ratio of more than 10, whereas in group 3 only 5 out of 29 patients had such a high ratio. Thus most of the patients in group 2 could be identified by their abnormal steroid excretion (*Fig.* 1). Two patients in group 2 died of heart failure and kidney failure respectively and these did not have any marked abnormalities in steroid excretion.

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DISCUSSION

The results indicate that it is possible to identify using a chemical method, even before surgical treatment, those lung cancer patients who have a poor prognosis despite resection of their lung tumours. The significance of these findings could be considerable in the management of these patients if it can be established that their abnormalities are of aetiological significance and are not merely a reflection of the stage of the disease. The latter possibility arises because in patients with inoperable lung cancer the same steroid abnormalities are significantly related to the prognosis (Rao and Hewit, 1970). Thus, in these patients the greater the 17-OHcs : A ratio the shorter is the survival time. The present results show that this ratio is equally useful in predicting the 1-year survival in patients whose lung tumours have been surgically removed. Therefore, it is possible that the 17-OHcs : A ratio indicates the presence of metastases which were not clinically recognizable, and thus reflects only the stage of the disease. An alternative possibility in surgically treated patients is that a high 17-OHcs : A ratio indicates a greater susceptibility to metastasis after surgery. Previous work (Rao, 1970) has shown that removal of the lung tumour does not result in the disappearance of these steroid abnormalities and therefore they cannot be considered as being due to the presence of the lung tumours. It is not likely that these abnormalities are the effects of the clinically unrecognizable secondary tumours, since the removal of the primary tumour did not result in the decrease of the abnormalities. Therefore it appears that these abnormalities in lung cancer are the characteristics not of the tumour but rather of the host, which may be involved in the defence against the growth and spread of the tumour. Some indications are already available of the possible ways in which steroid abnormalities may be involved in the defence mechanisms of the host against the tumour. These can be considered under three main aspects.

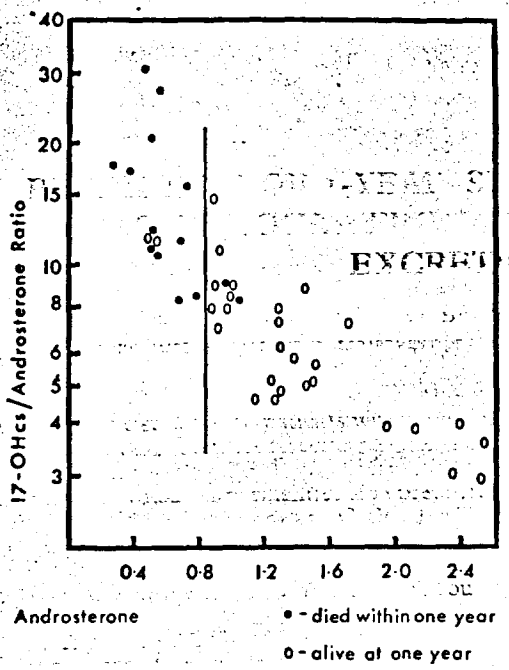

FIG. 1.—The survival of surgically treated patients.

1. Metabolic Effects.—Corticosteroids are mainly catabolic (Symington, 1969) and androsterone is anabolic (Furman and Howard, 1959). The high 17-OHcs : A ratio found in patients with a poor prognosis might shift the metabolic balance towards increased catabolism and lead to the cachexia found in many patients with a poor prognosis.

2. Haemostatic Effects.—It is known that cancer patients have an increased coagulability of their blood and this has been suggested as favouring the establishment of blood-borne metastasis (Thornes, 1967). Evidence for this view has come from the finding that the death-rate from cancer among persons receiving anticoagulant therapy is significantly lower than that in the general population (Thornes, 1967). It is known that corticosteroids increase coagulation by increasing the free fatty acids in the blood (Hoak and Robinson, 1963), whereas androsterone reduces coagulation by its ability to reduce platelet stickiness (Dufault, Tremblay, Nowaczynski, and Genest, 1961) and to increase fibrinolysis (Thornes, 1970). In fact, androsterone has been used prophylactically for this purpose in cardiovascular disease. Aetiocholanolone administration results in the increase of fibrinogen (Kimball, Vogel, Perry, and Wolff, 1967) and may thus enhance the tendency to coagulation. Thus, the low A : E ratio found in patients with a poor prognosis might have resulted in increased blood coagulation, favouring the establishment of blood-borne metastasis. Increased coagulability may also result in the formation of fatal pulmonary emboli.

3. Immunological Effects.—The importance of immunological mechanisms in the defence against cancer is now widely recognized (Editorial, *British*

Table I.—PREOPERATIVE STEROID EXCRETION IN GROUPS 1, 2, AND 3

GROUP	NO. OF PATIENTS	STEROID EXCRETION (mg. per g. creatinine per litre)			
		A	E	KS	17-OHcs
1	5	1·29 ± 0·46	2·90 ± 0·16*	7·02 ± 0·77	10·39 ± 3·56
2	16	0·72 ± 0·31*	1·19 ± 0·46*	4·18 ± 1·44*	8·26 ± 2·71
3	29	1·42 ± 0·66	2·11 ± 1·15	5·83 ± 1·93	8·11 ± 2·29

A, Androsterone; E, aetiocholanolone; KS, 17-oxosteroids; 17-OHcs, hydroxycorticosteroid.
* Significantly different from the mean of group 3 ($P < 0.01$).

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